REMARKS

Claims 1, 4-10, and 12-75 are currently pending. Claims 14-17 and 20-75 are withdrawn. Claims 2-3 and 11 are cancelled without prejudice. Applicants reserve the right to pursue subject matter from cancelled claims in a continuing application.

Claims 1, 4-10, 12-13, and 18-19 stand rejected.

Response to Specification Objections

The disclosure is objected to for the reference to "US 5,749,551[54]" which improperly cites the intended "US 5,759,551." Applicants have amended the specification to correct the inadvertent typographical error. As acknowledged by the Examiner, the endnote disclosed on page 13 supports the intended reference. Reconsideration and withdrawal of the objection to the specification are respectfully requested.

Response to Claim Objections

Claim 5 has been objected to for inconsistencies. Specifically, the phrases "cationic peptide immunogen" and "synthetic peptide immunogen" are not used consistently. The applicants have amended claim 5 with respect to these recitations for consistency, such that the claim now refers to "cationic peptide immunogen."

Claims 9-10 have been objected to for improper Markush-type language. Applicants respectfully disagree with the objection with respect to claim 9. Specifically, claim 9 recites: "X^1 is selected from the group consisting of A (adenine), G (guanine) and T (thymine)" which is in proper Markus-type language. However, with respect to claim 10, applicants have amended the claim accordingly.

Claims 9-10 have been further objected for allegedly being in improper dependent for failing to further limit the subject matter of a previous claim. Applicants respectfully disagree with the rejection. Specifically, the Examiner points to claim 1 (from which claim 9 depends) which requires the CpG oligonucleotide to have 8 to 64 nucleotide bases. Claims 9 and 10 each have specific CpG oligonucleotide formulas which are not indicated in claim 1. Applicants would like to also point out that these formulas have specific substitutions which are not disclosed in claim 1. Contrary to the Examiner's contention that

"the formulas recited in claims 9-10 is [sic] directed to include a CpG oligonucleotide that is 4 and 6 nucleic acid residues in length" (Office Action- page 4), claim 1 also states that "the number of repeats of the CpG motif is in the range of 1 to 10," thus claims 9 and 10 further limit the subject matter of claim 1.

Reconsideration and withdrawal of the objections to claims 5 and 9-10 are respectfully requested in view of the claim amendments and for the above reasons.

Response to Rejections under 35 U.S.C. §112, Second Paragraph

Applicants acknowledge the withdrawal of rejections to claims 7 and 18 under 35 U.S.C. §112, second paragraph in view of the previous claim amendments.

Rejections under 35 U.S.C. §103

The Examiner has maintained the rejections to claims 1, 5, 7-10, 12-13, and 18-19 under 35 U.S.C. §103(a) as being unpatentable over Krieg, et al. (WO 01/22972) in view of Ladd, et al. (WO 94/25060) as evidenced by result no. 1 of the rng and rag search summary pages. Applicants respectfully disagree with the Examiner's contention.

The Examiner contends that Krieg, et al. teach "a composition comprising an immunostimulatory nucleic acid and an anti-cancer therapy" (Office Action- page 7). In particular, the Examiner further contends that Krieg discloses an anionic CpG oligonucleotide which is identical to the instant SEQ ID NO:1. Specifically, Krieg's SEQ ID NO:429 "is a single stranded DNA of 32 nucleic acid residues in length having 5 repeats of a cytosine-guanine motif, and has a net negative charge of -32 at a pH in the range of 5.0-9.0" (Office Action- page 8). The Examiner further contends that SEQ ID NO:429 complies with the limitations of claim 10, directed to a formula of: 5' $(X^3)_2CG(X^4)_2$ 3' or 5' $X^3X^3CGX^4X^4$ 3', where X^3 is A or G and X^4 is C or T. However, applicants respectfully disagree with the Examiner's contention that SEQ ID NO:429 complies with the limitations of claim 10. Because the second instance of X^3 in Krieg's CpG motif: 5' (GT)CG(TT) 3' is not an A or G, but rather is a T, SEQ ID NO:429 does not comply with the limitations of claim 10.

The Examiner admits that Krieg, et al. do not teach the cationic peptide immunogen of the immunostimulatory microparticulate complex of the instant invention.

Specifically, Krieg does not disclose the use of a target B cell antigen or a CTL epitope and a T helper cell epitope as antigen. Moreover, as previously presented, Krieg's invention "relates in part to pyrimidine rich (Py-rich) and in some embodiments thymidine (T) rich immunostimulatory nucleic acids which do not require the presence of a CpG motif" (page 2, lines 17-19). Because Krieg also reports that pyrimidine rich (Py-rich) or TG nucleotides alone are sufficient to provoke an immune response (*See*, Page 2, lines 17-32 and Page 16, lines 23-32), Krieg actually suggests that the nucleotides alone are sufficient for evoking an immune response.

However, the Examiner contends that Krieg, in combination with Ladd, et al. which teach a cationic peptide immunogen capable of provoking an immune response, makes obvious the claimed invention. Applicants respectfully disagree with this contention.

Ladd, et al. report synthetic peptides capable of inducing antibodies against LHRH. In one embodiment, T helper cell epitopes are added to evoke an antibody response. However, there is no guidance or suggestion in Ladd for one skilled in the art to combine a cationic peptide immunogen with an anionic single-stranded DNA to form an immunostimulatory microparticulate complex. Without such motivation, and with Krieg suggesting the use of only an anionic polynucleotide, the skilled artisan would not have sufficient guidance to combine an anionic polynucleotide of Krieg and a cationic peptide immunogen of Ladd.

Applicants assert that there is no teaching, suggestion, or motivation in either Krieg or Ladd to combine a cationic peptide immunogen with an anionic polynucleotide. Applicants respectfully remind the Examiner that "[T]here must be a reason or suggestion in the art for selecting the procedure used, other than the knowledge learned from the applicants' disclosure" *In re Dow Chemical Co.*, 837 F.2d 469, 5 USPQ.2d 1529 (Fed. Cir. 1988) and "[n]eglect of the hindsight prohibition is reversible error" *Williams Service Group Inc. v. O.B. Cannon & Son Inc.*, 33 USPQ.2d 1705, 1726 n.11 (Pa. 1994). For the above reasons that there is no suggestion to combine the teachings of Krieg and Ladd, reconsideration and withdrawal of the 35 U.S.C. §103(a) rejections to claims 1, 5, 7-10, 12-13, and 18-19 are respectfully requested.

Claims 1, 4, and 6 are further rejected under 35 U.S.C. §103(a) as being unpatentable over Krieg, et al. in view of Ladd, et al. as applied to claim 1. Applicants respectfully traverse this rejection.

Regardless of whether the cationic peptide immunogen is a mixture of synthetic peptide immunogens, as presented above, Krieg and Ladd in combination do not disclose a microparticulate complex comprising 1) a cationic peptide immunogen of a target B cell antigen or a CTL epitope and a T helper cell epitope; and 2) an anionic CpG oligonucleotide having the specific parameters as disclosed in the instant claims. The Examiner further contends that at page 10 of the Office Action:

> it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use a mixture of peptide immunogens...to obtain an efficient immune response toward the reduction or suppression of LHRH levels in a mammal...[with] a reasonable expectation of success for doing so....

Even if it were prima facie obvious to use a mixture of peptide immunogens as the Examiner contends, it was not obvious to combine the anionic single-stranded DNA with a cationic peptide immunogen. Krieg states that its Py-rich or T-rich nucleic acids that do not contain CpG motifs are immunostimulatory. There is no suggestion, guidance, or motivation in either Krieg or Ladd to combine anionic single-stranded nucleic acids with a cationic peptide immunogen to result in the claimed immunostimulatory microparticulate complex. Therefore, reconsideration and withdrawal of this §103 rejection to claims 1, 4, and 6 are respectfully requested.

Dependent Claims

Applicants have not independently addressed all of the rejections of the dependent claims. Applicants submit that for at least similar reasons as to why independent claim 1 from which all of the dependent claims depend is believed allowable as discussed *supra*, the dependent claims are also allowable. Applicants however, reserve the right to address any individual rejections of the dependent claims and present independent bases for allowance for the dependent claims should such be necessary or appropriate.

Response to Double Patenting Rejection

Claims 1, 4-10, 12-13, and 18-19 are provisionally rejected the nonstatutory double patenting rejection as claiming the same invention as that of claims 1-8, 10-11, and 16-18 of copending application no. 10/355,161 (U.S. Publication No. 2004/0009897). Since the conflicting claims have not in fact been patented, this is a provisional statutory type double patenting rejection. However, applicants would like to point out that the instant invention is directed to an immunostimulatory microparticulate complex while the copending application (U.S. Application No. 10/355,161) is currently directed to a process for preparing a stabilized immunostimulatory complex. Claims 1-8, 10-11, and 16-18 of the copending application are withdrawn.

Applicants respectfully request that the provisional nonstatutory double-patenting rejection be held in abeyance due to the provisional nature of the rejection until one of the applications is allowed. Upon notice of otherwise allowable subject matter, applicants will address the rejection. Applicants note that it is proper when dealing with otherwise allowable subject matter in co-pending applications to withdraw a provisional rejection in the most advanced application, allow it to issue, and make a (non-provisional) rejection in the remaining applications.

CONCLUSION

It is believed that the claims 1, 4-10, 12-13, and 18-19 as presented herein are allowable. Thus, applicants respectfully submit that the invention as recited in the claims as presented herein is allowable over the art of record, and respectfully request that the respective rejections and objections be withdrawn.

AUTHORIZATION

Applicants believe that no additional fees are necessary, however, should any such fees be due, the Commissioner is hereby authorized to charge any additional fees which may be required for this Amendment, or credit any overpayment, to Deposit Account No. 13-4500, Order No. 1151-4172.

Respectfully submitted,
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Dated: December 19, 2006 By: _____

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